REMARKS

Claims 44-46 and 49-51 are currently pending in the application.

Claim Rejections - 35 USC §102

Claims 44-46, and 49-51 stand rejected under 35 USC §102(e) "as being anticipated by Lal et al. 5,942,606. The Examiner has indicated that the sole issue remaining in this application is whether or not Lal et al. is available as prior art.

Applicants maintain that the present application is entitled to the priority date of October 24, 1997, which precedes, by one month, the earliest priority date of Lal et al. (November 24, 1997). Accordingly, Lal et al. is not prior art against the present application, and this rejection should be withdrawn. Withdrawal of this rejection and allowance of this application is respectfully requested.

The Examiner acknowledges that Applicants have claimed priority to U.S. Provisional Patent Application No. 60/062,816 filed on October 24, 1997. The Examiner has denied benefit to the priority date of October 24, 1997 on the grounds that U.S.S.N. 60/062,816 does not meet the how-to-use requirement of 35 USC 112, first paragraph because prior to the disclosure of VEGF-inhibitory activity none of the asserted uses could be practiced without undue experimentation.

The Office Action states that Applicants cannot rely upon the similarity in structure to CAR to infer function and usefulness as a viral receptor. The art cited by the Examiner allegedly teaches that minor changes in structure can have major effects upon function in a virus receptor protein.

U.S. Patent Application No. 60/062,816 simply needs to disclose what is disclosed in the cited reference to support the priority claim

Appellants submit that U.S. Serial No. 60/062,816 simply needs to provide a disclosure commensurate in scope with the disclosure in the cited art to support the priority claim.

In In re Stempel (1957) 113 USPQ 77, the patent applicant (Stempel) had claims directed to both (i) a particular genus of chemical compounds (the "generic" claim) and

(ii) a single species of chemical compound that was encompassed within that genus (the "species" claim). In support of a rejection under 35 U.S.C. § 102, the examiner cited against the Stempel application a prior art reference that disclosed the exact chemical compound recited in Stempel's "species" claim. In response to the rejection, Stempel filed a declaration under 37 C.F.R. §. 1.131 demonstrating that he had made that specific chemical compound prior to the effective date of the cited prior art reference. The CCPA found Stempel's 131 declaration effective for swearing behind the cited reference for purposes of both the "species" claim and the "genus" claim. Specifically, the CCPA stated in support of its decision:

"We are convinced that under the law all the applicant can be required to show [in a declaration under37 C.F.R. §. § 1.131] is priority with respect to **so much of the claimed invention as the reference happens to show**. When he has done this he has disposed of the reference." (Id. at 81; emphasis supplied).

Secondly, the Examiner is respectfully directed to *In re* Moore, 170 USPQ 260 (CCPA 1971), where the Stempel rule was extended to cases where a reference disclosed the claimed compound but failed to disclose a sufficient utility for it. More specifically, the patent applicant (Moore) claimed a specific chemical compound called PFDC. In support of a rejection of the claim under 35 U.S.C. § 102, the examiner cited a reference which disclosed the claimed PFDC compound, but did not disclose a utility for that compound. Applicant Moore filed a declaration under 37 C.F.R. § 1.131 demonstrating that he had made the PFDC compound before the effective date of the cited prior art reference, even though he had not yet established a utility for that compound. On appeal, the CCPA indicated that the 131 declaration filed by Moore was sufficient to remove the cited reference. The CCPA relied on the established "Stempel Doctrine" to support its decision, stating:

An applicant need **not** be required to show [in a declaration under 37 C.F.R. § 1.131] any more acts with regard to the subject matter claimed that can be carried out by one of ordinary skill in the pertinent art following the description contained in the reference....the determination of a practical utility when one is not obvious need **not** have been accomplished prior to the date of a reference unless the reference also teaches how to use the compound it describes. (Id. at 267, emphasis supplied).

Thus, *In re* Moore confirms the Stempel rule holding that in order to effectively remove a cited reference with a declaration under 37 C.F.R. § 1.131, an applicant need only show that portion of his or her claimed invention that appears in the cited reference.

U.S. Patent Application No. 60/062,816 filed on October 24, 1997, provides the nucleic acid and amino acid sequence of the PRO246 polypeptide and indicates that this amino acid sequence shares significant homology to the human Coxsackie-adenovirus receptor (See U.S. Serial No. 60/062,816 at page 2, lines 8 -11). Considering its homology to the human Coxsackie adenovirus receptor, Applicants further suggest the PRO 246 polypeptide to be novel cell surface virus receptor.

Lal discloses a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application. It provides sequence homology with HCAR as support for the sequence being useful as a viral receptor (See Column 9, lines 56-59). The specification of the issued U.S. patent is devoid of any experimental data demonstrating the antiviral activity of ACVRP, or identifying the specific viruses associated with this receptor. It indicates that Northern analysis shows the expression of this sequence in various libraries, at least 65% of which are immortalized, cancerous or proliferating cells and at least 19% of which involve an inflammatory response (See Col. 9, lines 60-64). The Patent Office has granted **Lal**, U.S. Patent No. 5,942,606.

The disclosures are commensurate in scope. Appellants submit that the priority document discloses all that the cited prior art discloses and accordingly, Appellants should be entitled to their priority.

U.S. Patent Application No. 60/062,816 does contain sufficient information to enable one skilled in the art to practice the invention.

Appellants maintain that they are entitled to priority to U.S. Provisional Patent Application No. 60/062,816 with an effective filing date of October 24, 1997. Appellants submit that the priority document disclosure does provide sufficient information to enable one skilled in the art to practice the claimed invention.

The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what is already known, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation"" Amgen Inc. v. Hoechst Roussel, Inc. 65 USPQ2d 1385-1421, 1400 (Fed Cir 2003) citing Genentech, Inc. v. Novo Nordisk, A/S 42 USPQ2d 1001, 1004 (Fed Cir. 1997). "That some experimentation is necessary does not constitute a lack of enablement" Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ2d 1016, 1026. (Fed. Cir 1991).

U.S. Serial No. 60/062,816 filed on October 24, 1997, provides the nucleic acid and amino acid sequence of the PRO246 polypeptide and indicates that this amino acid sequence shares significant homology to the human Coxsackie-adenovirus receptor (See U.S. Serial No. 60/062,816 at page 2, lines 8 -11). Considering its homology to the human Coxsackie adenovirus receptor, Applicants further suggest the PRO 246 polypeptide to be novel cell surface virus receptor. (See page 2, lines 8 - 11, and page 24, lines 24 - 27). The specification provides in Example 1 (pages 23 - 24) the method used to identify and clone the PRO 246 sequence. The specification provides other methods which could be used to obtain the PRO246 polynucleotide (page 8, line 25 - page 9, line 23). The specification provides methods which could be used for selecting and using a vector for the expression of PRO 246 and methods which could be used for selecting and transforming host cells with PRO246. (See pages 9 - 13, Examples 3-6). The specification sets forth a number of different uses for the nucleotide sequences encoding PRO 246 polypeptides at, for example, pages 14 - 17. Such uses include use of the extracellular domain of the PRO 246 polypeptide therapeutically *in vivo* for lessening the effects of viral infection and the use of PRO246 polypeptides as therapeutic targets for anti-tumor drugs.(page 17, lines 9 - 15)

It was known in the art at the earliest priority date of the present application that HCAR is a human cellular receptor for the group B Cocksackie-viruses (CVB), and human subgroup C adenoviruses (Ad2 and Ad5) (see Tomko *et al.,* (April 1997) *Proc. Natl. Acad. Sci. USA* 94:3352-3356; See also U.S. Serial No. 60/062,816 at page 1)). It

was also well known that the Coxsackie-virus is involved in a variety of diseases, most prominently, human myocarditis (Tomko et al., page 3356, column 2). [1]

1. The Patent Office states that Appellants cannot rely upon the similarity in structure to CAR to infer function and usefulness as a viral receptor. The art cited by the Patent Office allegedly teaches that minor changes in structure can have major effects upon function in a virus receptor protein. In support of this argument, the Examiner states that alignment of Applicants' sequence with the human and mouse CAR proteins indicates an overall similarity of 17% and a best local similarity of 27%. The Examiner, in the Office Action dated May 20, 2003 cited McNicholl *et al.*, (1997) *Emerging Infectious Diseases*, 3(3):261 as evidence that a protein with 100% homology to a portion of a virus receptor does not function as a virus receptor and Struyf *et al.*, (2002) *J. Virology*, 76(24):12940 that alteration of even a few amino acids degrades the ability of another receptor to interact with virus.

Appellants note that both McNicholl *et al.*, and Struyf *et al.*, teach and disclose experiments altering a naturally occurring receptor. They are not comparing two receptors. If certain alterations are made to a protein it can be rendered inactive. Such papers are not probative of whether a newly identified viral receptor, similar to the known CAR receptor, must be highly homologous to the CAR receptor in order to be functional.

The Examiner In the Office Action dated May 20, 2003, cited Carson (2001) *Reviews in Medical Virology* 11(4):219-26 (abstract only), as evidence that the N-terminal region of CAR physically complexes with adenovirus. Cohen *et al.*, (2001) *J. Biological Chemistry* 276(27):25392-25398, was cited as evidence that the C-terminal region of CAR is not required for adenovirus receptor activity. The Examiner indicates that this allegedly non-essential C-terminal region of CAR is the region most homologous to Appellant's protein.

The PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure, only after the PTO provides evidence showing that one of

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[1] A copy of the Tomko reference was previously provided.

ordinary skill would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence. In re Brana 51 F.3d 1560, 34USPQ2d 1436 (Fed. Cir. 1995)

> "The PTO has not satisfied its initial burden. Accordingly, applicants should not have been required to substantiate their presumptively correct disclosure to avoid a rejection under the first paragraph of § 112".

The Patent Office has failed to meet its burden. First, the Patent Office has not provided any percentage homologies to support its finding that the C-terminal region is the most homologous. Secondly, even if the C-terminal region is the most homologous this does not provide evidence that the PRO246 polypeptide cannot act as a viral receptor.

2. The Patent Office indicates a failure to see where Tomko provides evidence of general knowledge in the art to discover a virus bound to the hypothetical receptor. Further, the priority document allegedly does not identify any specific virus which interacts with the viral receptor, requiring those skilled in the art to perform experimentation to discover a specific use for this protein.

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. In re Wands 858 F.2d 731, 737. "That some experimentation is necessary does not constitute a lack of enablement." Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ 2d 1016, 1026 (Fed. Cir 1991).

U.S. Serial No. 60/062,816 at Examples 3 and 4 provides methods for transforming prokaryotic and eukaryotic cells and methods of expressing the gene in prokaryotic and eukaryotic cells.

Appellants note that Tomko et al. provides a general virus assay on page 3352. Tomko provides a method for transfecting NIH3T3 cells with a plasmid expressing the receptor (page 3352). Tomko et al. provides a virus assay to be conducted with different viruses on the transformed cells (page 3352). Clearly such assays were well known in the art and could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor.

3. Finally, the Patent Office argues that Appellants cannot rely on U.S. 5,942,606, as *prima facie* evidence that Appellants ' priority document, U.S. Serial No. 60/062,816 is sufficient to teach those skilled in the art to make and use the claimed invention without undue experimentation.

Appellants cite U.S. Patent No. 5,942,606 as evidence that Appellants priority document specification does not require undue experimentation having due regard for the nature of the invention and the state of the art.

U.S. Patent No. 5,942,606 discloses a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application. It provides sequence homology with HCAR as support for the sequence being useful as a viral receptor (See Column 9, lines 56-59). The specification of the issued U.S. patent is devoid of any experimental data demonstrating the antiviral activity of ACVRP, or identifying the specific viruses associated with this receptor.

Firstly, the Patent Office has issued U.S. Patent No. 5,942,606 and thus under 35 USC 262, there is a presumption that the patent is fully enabled. Clearly the Patent Office believes U.S. Patent No. 5,942,606 to provide both enablement and utility for the compounds disclosed.

Appellants are simply making the argument that U.S. Serial No. 60/062,816 has a very similar disclosure to **Lal**, U.S. Patent No. 5,942,606, which presumptively meets both the utility and enablement requirements of the statute.

Accordingly, if U.S. 5,942,606 is fully enabled, which the Patent Office has determined, then Appellants priority document is similarly fully enabled.

<u>U.S. Patent Application No. 60/062,816 discloses an inherent utility to support the priority claim</u>

The Patent Office alleges that the specification Of U.S. Patent Application No. 60/062,816 does not provide sufficient information on the function and usefulness of the PRO246 polynucleotide.

As indicated above Appellants maintain that U.S. Patent Application No. 60/062,816 does disclose sufficient function and usefulness to support the priority claim. Appellants submit that although U.S. Provisional Patent Application No. 60/062,816

does provide sufficient direct disclosure of utility, it is sufficient for a priority application to merely disclose the compounds with sufficient detail to enable one skilled in the art to make them. The function and usefulness of the compound can be inherent.

It is understood that conception of an invention is not complete absent a conception of its utility. However, the courts have held that when a claim fully identifies the compound and the property is inherent in the compound, the recitation of that property does not add anything to the claim. In re Ruschig 343 F.2d 965 (CCPA 1965. Further in Rey-Bellet v. Engelhardt 493 F.2d 1380 (CCPA 1974) the court held that structural similarity of the claimed compounds to prior art compounds having a known use made it unnecessary to corroborate conception of utility.

The possibility of inherent conception is recognized in Silvestri v. Grant 496 F.2d 593 (CCPA 1974). In Silvestri the court held that it was not necessary to actually determine the molecular weight of ampicillin (recited in the claims) since it was an inherent property of the molecule. The court stated, "where the balance of the claim fully identifies the compound ...and the property is inherent, we fail to see that such statements add anything to the claim definition of the named compound."

The Court in Hitzeman v. Rutter 58 USPQ2d 1161 (Fed. Cir. 2001) has indicated that to invoke the "inherent conception" rule of Silvestri,

> "the inventor needs to show that the allegedly inherent property adds nothing to the count beyond the other recited limitations, and is redundant to the count...In the context of priority determinations, the allegedly inherent limitation cannot be material to the patentability of the invention. Moreover, **consistent with the law of inherent anticipation**, an inherent property must necessarily be present in the invention described by the count, and it must be recognized by persons of ordinary skill in the art." (emphasis added)

Recent case law in the area of inherent anticipation has held that if a person of ordinary skill in the art, presented with all facts, would understand that the missing structure, composition or function is always necessarily present in the cited prior art, a holding of anticipation by inherency is proper. It is not required that prior to the invention one skilled in the art recognized the presence of the inherent structure, composition or function. The objective understanding of the presence of the inherent structure, composition or function can occur later. Atlas Powder Co. v. Ireco Inc. 190

F.3d 1342; 51 USPQ2d 1943 (Fed. Cir. 1999); Schering Corporation v. Geneva Pharmaceuticals, Inc. 67USPQ2d 1664 (Fed. Cir 2003). Pursuant to this line of cases, Appellants should be entitled to claim priority to U.S. Patent Application No. 60/062,816 because the function of the PRO 246 polynucleotide is inherent in the compound.

U.S. Patent Application No. 60/062,816 filed on October 24, 1997, provides the nucleic acid and amino acid sequence of the PRO246 polypeptide and indicates that this amino acid sequence shares significant homology to the human Coxsackie-adenovirus receptor (See U.S. Serial No. 60/062,816 at page 2, lines 8 -11). Considering its homology to the human Coxsackie adenovirus receptor, Applicants further suggest the PRO 246 polypeptide to be a novel cell surface virus receptor. Accordingly, Applicants go beyond the requirements for inherent utility in that Applicants disclose the utility in the priority document.

Lal discloses a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application. It provides sequence homology with HCAR as support for the sequence being useful as a viral receptor (See Column 9, lines 56-59). The Patent Office has granted Lal et al., U.S. Patent No. 5,942,606 and clearly accepts that this sequence has inherent utility as a viral receptor.

Consistent with the line of cases cited above, Appellants should be entitled to priority to U.S. Patent Application No. 60/062,816.

Finally, Appellants submit that they have provided in U.S. Patent Application No. 60/062,816 a disclosure very similar to that of **Lal**. **Lal** was granted a patent based on its disclosure. Appellants submit that they are unfairly being held to a different standard of patentability than that applied to the **Lal** patent application. It is the most important principle of U.S. patent law that a patent on a given invention must be granted to the person or persons who were first to invent that invention. In the present case, there is clear evidence suggesting that Applicants were first to invent the PRO246 polypeptide and all related subject matter, yet a patent was granted to a different group of inventors, and until the claims pending in the present application are allowed, Applicants have no recourse to remedy this inequitable outcome. It is legally wrong and inequitable to hold Applicants to a different, more stringent, standard of patentability, solely as a result of recent changes in the Patent Office's application of the requirements of patentability.

In conclusion, Appellants should be entitled to the priority of U.S. Provisional Patent Application No. 60/062816 with a priority date of October 24, 1997, which precedes, by one month, the earliest priority date of **Lal** (November 24, 1997). Accordingly, **Lal** is not prior art against the present application and the rejection of claims 44-46, and 49-51 should be withdrawn.

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding, she is invited to contact the undersigned attorney at the telephone number shown below.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-1618 P2C21**).

Respectfully submitted,

Date: August 25, 2004

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8/25/04 10:40 AM (39780.1618)